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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

GUCKER, STEPHEN

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/564,819	Applicant(s) OKAZAKI, HIROSHI	
	Examiner STEPHEN GUCKER	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-60 is/are pending in the application.
- 4a) Of the above claim(s) 19-23 and 33-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 and 24-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/13/06, 2/27/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-18 and 24-32 in the reply filed on 4/27/09 is acknowledged. The traversal is on the ground(s) that Shi et al. did not anticipate the invention of Group I and therefore the different groups have unity of invention. This is not found persuasive because of the prior art rejections made in this Office Action.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 19-23 and 33-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/27/09.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-6, 8, 10-11, 13-18, 24-25, 27-28 and 30-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of claim 1 wherein the FGF is bFGF, does not reasonably provide enablement for all FGFs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state

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of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to methods of obtaining a self-renewing undifferentiated population of oligodendrocyte precursor cells comprising culturing oligodendrocyte precursor cells in a medium comprising an effective amount of a fibroblast growth factor (FGF) in substantial absence of platelet-derived growth factor (PDGF). The specification discloses in Examples 1 and 2 that the aforementioned was achieved by replating precursor cells grown from rat embryonic spinal cord (E14-E19) or fetal human brain tissue and spinal cord (9-10 weeks) in DMEM/N2 medium with 25 ng/ml PDGF, 15 ng/ml bFGF, 5ng/ml NT-3, and 0.05% bovine serum into a medium comprising DMEM/B27, 10 μ M 3,3',5'-triiodothyronine (T3), and 10 ng/ml bFGF, and finally replating said precursors again into a medium comprising DMEM/B27 and 15-30 ng/ml bFGF. However, bFGF (basic FGF also known as FGF2) is separate and distinct from other FGFs.

With at least fourteen similar but distinct ligands, four receptors and their multiple isoforms, plus an extended family of coreceptors, it is clear that a cell has ample opportunity to modulate its response to FGFs by regulating the combinatorial complexity of a diverse set of cell surface receptors (IDS filed 2/27/07, reference C5, Bansal et al. 1997 page 215).

Thus, the complex nature of the invention and the wide breadth of the claims is not commensurate in scope with the supporting disclosure or the prior art.

State of the prior art and level of predictability in the art: The art teaches that the effect of even just bFGF on oligodendrocyte precursors was not predictable without substantial

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experimental work which was neither routine or predictable. The nature of the response of precursor oligodendrocytes to bFGF varied markedly as a function of the stage of development of the oligodendrocyte lineage. bFGF upregulates PDGF receptors on early progenitors, and with PDGF supports their long-term proliferation; bFGF is mitogenic for late progenitors and reversibly blocks their terminal differentiation; bFGF can even cause an apparent phenotypic reversion of mature oligodendrocytes (IDS filed 2/27/07, reference C4, Bansal et al. 1996, pages 263-264).

Thus, the art relevant to actually using just bFGF of the instant invention demonstrates a complex biological system with many interactions, hence the invention is innately unpredictable as well.

Amount of direction provided by the inventor and existence of working examples: The working examples disclosed are all limited to using bFGF and not any other isoform of FGF is used. Further, it is not a matter of simply culturing precursor cells in a medium with any FGF and without PDGF directly that produces the limitations recited in the methods, but a three step procedure first using PDGF, NT-3, bovine serum and bFGF (15 ng/ml), then omitting PDGF, NT-3, bovine serum but including T3 and bFGF (10 ng/ml), and finally including only bFGF (15-30 ng/ml) in the medium. No direction is provided that distinguishes the use of other FGFs for when and how much should be employed in the instant methods other than what is disclosed for bFGF.

Thus, the disclosure provides no validation that a method using other FGFs will be enabled to produce a self-renewing oligodendrocyte precursor.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to make and use the invention as asserted in the application without undue experimentation to establish the use of other FGFs as being essentially similar to bFGF since the instant disclosure does not teach any differences between the use of bFGF and other FGFs.

Given this high degree of unpredictability and the absence of any evidence to indicate that the methods of the instant invention are effective with other FGFs other than bFGF, the use of other FGFs (and what amounts, patterns, and durations of use produce the recited results) is no more than a theoretical possibility. This is not sufficient to meet the enablement requirement of 35 USC §112, first paragraph.

In view of the foregoing, using the invention as claimed would require undue experimentation. Therefore, the claims are properly rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure commensurate with the instant claims.

5. Claims 7, 12, and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 7 recites that the homogeneous population of oligodendrocyte precursor cells are restricted to the oligodendrocyte lineage. However, as the prior art from Bansal et al. demonstrated above, a precursor cell's lineage is dependent upon its age and specific culturing conditions involving a specific pattern and amount of growth factors, and not the precursor cell itself, and the

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instant specification does not provide adequate guidance or direction to put such a cell as claimed into the hands of the public without undue experimentation. Similarly, it cannot be predicted from either the teachings of the prior art or the instant disclosure that using only an unvarying concentration of 5 ng/ml of bFGF would produce the results as required by the claim limitations because of the complex and unpredictable nature of the invention for the reasons already of record.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-6, 8-11, 13-18, 24-28 and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Bansal et al. 1996 ("Bansal 1996"). Bansal teaches a method of culturing oligodendrocyte progenitors from neonatal rat telencephalon with 10 ng/ml of bFGF without PDGF to produce what Bansal calls "late progenitors" and mature oligodendrocytes (page 273). Bansal notes the synchronizing effects of bFGF, and late progenitors are mostly A2B5(+)O4(+)O1(-), but some are A2B5(+)O4(+)O1(+) (see pages 264-265 and Figure 1). With regards to claim 18, the prior art meets these limitations because the prior art cells "have the ability" to meet the limitations because the limitations are dependent on further culturing conditions as taught by the prior art and the instant disclosure. Similarly, the prior art meets the limitations of claim 2 because they "are culturable" for at least about one year without phenotypic change as long as they remain in a medium comprising bFGF and without PDGF.

8. No claim is allowed.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. G./

Examiner, Art Unit 1649

Stephen Gucker

September 3, 2009

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649